Research

An mRNA vaccine delivered in hydrogel shows promise as a durable cancer immunotherapy

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Chinese scientists have developed a hydrogel that can slowly release an mRNA vaccine over time to to trigger long-lasting antitumor immune responses, they reported. (Getty Images)

Before mRNA vaccines became valuable preventive tools against COVID-19, scientists around the world were studying the technology's potential use in cancer therapeutics, but their success has, so far, been limited.

Now, scientists at China's National Center for Nanoscience and Technology (NCNST) have designed a hydrogel to deliver an mRNA vaccine with an immune-stimulating adjuvant. When injected into mice with melanoma, the vaccine stayed active for at least 30 days, inhibiting tumor growth and preventing metastasis, according to

lasting anti-tumor effects as cancer immunotherapy, the researchers said.

In COVID-19, mRNA vaccines carry the genetic information that instructs the body to produce a specific viral protein to trigger the desired immune response. In cancer, the vaccines are typically designed to translate tumor-associated antigens so the immune system can recognize and eliminate the cancer.

Problem is, RNA is very unstable, and mRNA vaccines must reach the lymph nodes to work. For its FDA-authorized COVID-19 shot Comirnaty (BNT162b2), BioNTech used small particles of fat known as lipid nanoparticles to protect the core mRNA information. The nanoparticles degrade and release the mRNA once they reach the target tissue. The mRNA itself also quickly degrades after protein translation.

That short immune engagement works to prevent COVID-19, but, in cancer treatment, a more long-lasting delivery of mRNA would be required to achieve stable therapeutic outcomes.

For that purpose, the NCNST team designed a hydrogel with graphene oxide and low-weight polyethylenimine. The graphene oxide can efficiently load drug substances thanks to its large surface area, and the polyethylenimine binds the mRNA content for translation. To further enhance the stimulation and expansion of antigen-specific CD8+ T cells—which are critical for anti-tumor immune responses—in the presence of a hostile tumor microenvironment, the team added Galderma's TLR7/8 agonist resiquimod as an adjuvant.

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To test their mRNA platform, the researchers used ovalbumin, a protein found in chicken egg whites, as a model antigen. They mixed ovalbumin mRNA and the adjuvant with the hydrogel and injected it under the skin of mice with melanoma tumors engineered to express ovalbumin on their surface.

The hydrogel steadily released the vaccine—including both the mRNA and the adjuvant—in nanoparticles for at least 30 days, and it migrated to lymph nodes, the team showed.

The animals that received just one injection of the complete therapy had significantly smaller tumors compared with mice that got free adjuvant and the mRNA without the hydrogel, or those that received a nonadjuvanted mRNA hydrogel. Mice that got the complete therapy also exhibited the highest number of CD8+ T cells that entered tumors, the scientists found.

What's more, the novel mRNA gel treatment induced the highest level of ovalbumin-specific antibodies in the serum compared with others, suggesting it not only inhibited the growth of tumors but also prevented tumors from returning or forming distant metastasis. Indeed, there were no observable metastases in the lung tissues of mice that got the complete regimen, while the free mRNA-adjuvant combo and the nonadjuvanted mRNA gel solution only partially alleviated metastases when compared with control mice that got saline or only the gel delivery system, the scientists reported.

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The biopharma companies that sped mRNA COVID-19 vaccines to market are still interested in applying the technology to cancer. But it's early days, and they've encountered plenty of hurdles.

BioNTech and collaborator Roche reported a mere 8% response rate in 108 phase 1b trial patients who received

The NCNST team suggests its hydrogel system holds potential as an efficient mRNA platform for use in cancer immunotherapy. “Collectively, the present study demonstrates the great potential of the GLP-RO Gel in achieving durable and efficient cancer immunotherapy,” the researchers wrote in the study.

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